UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/594,358	11/26/2007	Trent Martin Woodruff	529282002400	4642

25225 7590 10/15/2008

MORRISON & FOERSTER LLP
12531 HIGH BLUFF DRIVE
SUITE 100
SAN DIEGO, CA 92130-2040

EXAMINER	
NIEBAUER, RONALD T	

ART UNIT	PAPER NUMBER
1654	

MAIL DATE	DELIVERY MODE
10/15/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/594,358	WOODRUFF ET AL.	
	Examiner	Art Unit	
	RONALD T. NIEBAUER	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *17 June 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-28* is/are pending in the application.

4a) Of the above claim(s) *6,7,19-22,25 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8-18,23,24,27 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date 9/4/07.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of the following species:

Inhibitor compound: PMX53, illustrated in Figure 1 wherein A is NH-acyl, B is benzyl, C is the sidechain of L-proline, D is the sidechain of D-cyclohexylalanine, E is the sidechain of L-tryptophan, F is the sidechain of L-arginine, and X1 is –(CH2)3NH-

Disease: Parkinsons disease

Other agent: infliximab

in the reply filed on 6/17/08 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Applicant states that claims 1-5,8-18,23-24,27-28 read on the elected invention. Although unclear (see 112 2nd) claims 1-5,8-18,23-24,27-28 are interpreted as reading on the elected invention.

Claims 6-7,19-22,25-26 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 6/17/08.

Claims 29-31 have been cancelled.

Claims 1-5,8-18,23-24,27-28 are under consideration

In the instant case, each of the elected species was found in the prior art. Any prior art that reads on non-elected species (or only on some but not all of the species) that was uncovered

in the course of searching for the elected species is also cited herein. In accord with section 803.02 of the MPEP the claims have been examined to the extent necessary to determine patentability.

Claim Objections

Claims 12,15-17 are objected to because of the following informalities:

Claim 12 recites the abbreviation C5aR. The abbreviation is described in the specification (page 3 line 4) but should be identified the first time it is used in the claims. Further, claim 12 recites 'no C5a agonist activity'. It appears that the word 'receptor' is missing after the word 'C5a', since it is the receptor activity that is measured.

Claim 15 refers to compounds described in PCT/AU02/01427. Claims 16 and 17 refer to compounds such as PMX53. Section 2173.05(s) of the MPEP states that 'Where possible, claims are to be complete in themselves'. In the instant case, the claims are not complete as the identity of the compounds is not evident from the claims.

Further, the identity of the abbreviations PMX53 and AcF[OP-DCha-WR], for example, should be set forth to clearly identify the compounds. For example, O is not a standard abbreviation used when referring to amino acids. For example, page 21 line 35 sets forth that O is Orn.

Appropriate correction is required.

Specification

The disclosure is objected to because of the following informalities:

The disclosure is objected to because it contains an embedded hyperlink and/or other form of browser-executable code. Applicant is required to delete the embedded hyperlink and/or other form of browser-executable code. See MPEP § 608.01.

In the instant case, page 18 line 20 includes an embedded hyperlink.

Appropriate correction is required.

The incorporation of essential material in the specification by reference to an unpublished U.S. application, foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference, if the material is relied upon to overcome any objection, rejection, or other requirement imposed by the Office. The amendment must be accompanied by a statement executed by the applicant, or a practitioner representing the applicant, stating that the material being inserted is the material previously incorporated by reference and that the amendment contains no new matter. 37 CFR 1.57(f).

The attempt to incorporate subject matter into this application by reference to PCT/AU98/00490 and PCT/AU02/01427 (see page 21 lines 30-31) is ineffective (see MPEP section 608.01(p) I.). Claim 15 also refers to PCT/AU02/01427 (but does not used the words incorporate and reference see 37 CRF 1.27(b)(1)) and compounds that are described therein.

37 CFR 1.57(c) states that

> " Essential material " may be incorporated by reference, but only by way of an incorporation by reference to a U.S. patent or U.S. patent application publication, which patent or patent application publication does not itself incorporate such essential material by reference.

In the instant case, the identity of the compounds described in claim 15 are essential material since a description of the compounds is needed to provide written description and to distinctly claim the invention.

The incorporation by reference will not be effective until correction is made to comply with 37 CFR 1.57(b), (c), or (d). If the incorporated material is relied upon to meet any outstanding objection, rejection, or other requirement imposed by the Office, the correction must be made within any time period set by the Office for responding to the objection, rejection, or other requirement for the incorporation to be effective. Compliance will not be held in abeyance with respect to responding to the objection, rejection, or other requirement for the incorporation to be effective. In no case may the correction be made later than the close of prosecution as defined in 37 CFR 1.114(b), or abandonment of the application, whichever occurs earlier.

Any correction inserting material by amendment that was previously incorporated by reference must be accompanied by a statement that the material being inserted is the material incorporated by reference and the amendment contains no new matter. 37 CFR 1.57(f).

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 3-5,8-11,15-17 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 3 and dependent claims refer to a compound that 'has substantially no agonist activity'.

The term 'substantially' in claim 3 is a relative term which renders the claim indefinite. The term 'substantially' is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 3 and dependent claims refer to peptidomimetics of formula I.

The term 'peptidomimetic' in claim 3 is a relative term which renders the claim indefinite. The term 'peptidomimetic' is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The term 'bioisostere' in claim 3 is a relative term which renders the claim indefinite. The term 'bioisostere' is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claim 3 and dependent claims refer to X1 in formula 1 but do not give any conditions for X1. However, there are conditions provided for X. As such, it is unclear if X1 is the same as X. There is more than one reasonable interpretation of the claim: X1 has no limitation or X1 is X.

Claims 15-17 refer to compounds that are described in PCT/AU02/01427 and refer to compounds such as PMX205. The elected species is described as PMX53, illustrated in Figure 1 wherein A is NH-acyl, B is benzyl, C is the sidechain of L-proline, D is the sidechain of D-

cyclohexylalanine, E is the sidechain of L-tryptophan, F is the sidechain of L-arginine, And X1 is –(CH2)3NH-.

The attempt to incorporate subject matter into this application by reference is discussed above. Also, the claims are not complete in themselves as discussed above.

Applicant states that the elected species is PMX53 is illustrated in figure 1 with A being NH-acyl. However, there is no Nitrogen at the A position for the compound identified as PMX53 in Figure 1.

Taylor et al (WO 03/033528 as cited in the IDS) is the international publication of international application PCT/AU02/01427 which applicant refers to in claim 15. Compound 1 is shown on page 33 of WO 03/033528 and page 18 lines 7-8 state that it is PMX53. However, compound 1 (i.e PMX53) on page 33 of WO 03/033528 is different from PMX53 as shown in figure 1 of the instant invention. In particular PMX53 as shown in figure 1 of the instant invention has no Nitrogen at the A position, while PMX53 on page 33 of WO 03/033528 has a Nitrogen at the A position. As such, the identity of PMX53 is unclear.

Further, neither page 33 of WO 03/033528 or Figure 1 of the instant invention clearly set forth the X variable. In particular, one can not ascertain from the drawings what 'n' is.

The identity of the abbreviations PMX53 and AcF[OP-DCha-WR], for example, should be set forth to clearly identify the compounds. For example, O is not a standard abbreviation used when referring to amino acids.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-5,8-18,23-24,27-28 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The MPEP states that the purpose of the written description requirement is to ensure that the inventor had possession, as of the filing date of the application, of the specific subject matter later claimed by him. The courts have stated:

> "To fulfill the written description requirement, a patent specification must describe an invention and do so in sufficient detail that one skilled in the art can clearly conclude that "the inventor invented the claimed invention." Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997); In re Gostelli, 872 F.2d 1008, 1012, 10 USPQ2d 1614, 1618 (Fed. Cir. 1989) ("[T]he description must clearly allow persons of ordinary skill in the art to recognize that [the inventor] invented what is claimed."). Thus, an applicant complies with the written description requirement "by describing the invention, with all its claimed limitations, not that which makes it obvious," and by using "such descriptive means as words, structures, figures, diagrams, formulas, etc., that set forth the claimed invention." Lockwood, 107 F.3d at 1572, 41 USPQ2d at 1966." Regents of the University of California v. Eli Lilly & Co., 43 USPQ2d 1398.

Further, for a broad generic claim, the specification must provide adequate written description to identify the genus of the claim. In *Regents of the University of California v. Eli Lilly & Co.* the court stated:

> "A written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Fiers*, 984 F.2d at 1171, 25 USPQ2d 1601; *In re Smythe*, 480 F.2d 1376, 1383, 178 USPQ 279, 284985 (CCPA 1973) ("In other cases, particularly but not necessarily, chemical cases, where there is unpredictability in performance of certain species or subcombinations other than those specifically enumerated, one skilled in the art may be found not to have been placed in possession of a genus ...") *Regents of the University of California v. Eli Lilly & Co.*, 43 USPQ2d 1398.

The MPEP further states that if a biomolecule is described only by a functional characteristic, without any disclosed correlation between function and structure of the sequence, it is "not sufficient characteristic for written description purposes, even when accompanied by a method of obtaining the claimed sequence." MPEP § 2163. The MPEP does state that for a generic claim the genus can be adequately described if the disclosure presents a sufficient number of representative species that encompass the genus. MPEP § 2163. If the genus has a substantial variance, the disclosure must describe a sufficient variety of species to reflect the variation within that genus. See MPEP § 2163. Although the MPEP does not define what constitute a sufficient number of representative species, the courts have indicated what do not constitute a representative number of species to adequately describe a broad generic. In *Gostelli*, the courts determined that the disclosure of two chemical compounds within a subgenus did not describe that subgenus. *In re Gostelli*, 872, F.2d at 1012, 10 USPQ2d at 1618.

The MPEP lists factors that can be used to determine if sufficient evidence of possession has been furnished in the disclosure of the Application. These include "level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention. Disclosure of any combination of such identifying characteristics that distinguish the claimed invention from other materials and would lead one of skill in the art to the conclusion that the applicant was in possession of the claimed species is sufficient." MPEP § 2163. While all of the factors have been considered, a sufficient amount for a *prima facie* case are discussed below.

In the instant case, the claims are drawn to a methods or treatment. The agent used to treat is broadly described as an inhibitor (claim 1) and is also described by functional properties (claims 3,12-14,18. The inhibitor is described as a peptidomimetic of formula I (claim 3b). As discussed above (see 112 2nd), the claims are unclear. For purposes of examination, the claims have been given the broadest reasonable interpretation.

(1) Level of skill and knowledge in the art:

The level of skill in the art is high.

(2) Partial structure:

The agent used for treatment is described as an inhibitor (claim 1) and is also described by functional properties (claims 3,12-14,18). It is noted that claims 1-2, for example, are not limited by any recited structure. In fact, the inhibitor is not limited to any size and does not even have to be cyclic or even a peptide. Hence there is substantial variability in the genus. However, the specification appears to be drawn to inhibitors of formula I. One would not recognize that cyclic peptides of formula I are representative of any and all inhibitors of C5a activity.

Claim 3 recites that the compound is a peptidomimetic of formula I. As discussed above, the scope of peptidomimetic is unclear. For purposes of examination, peptidomimetic has been given its broadest interpretation. It is noted that the claims state that the compound is s peptidomimetic of Formula I and as such does not necessarily have to be of formula I. Although claims 5,8-11,15-17 recite alternates at specific positions or refer to specific compounds, the claims remain open to peptidomimetics of those compounds. As such, any compound that shares any similar sequence, for example a single amino acid residue or functional group, is considered a mimic and falls within the scope of the claims. For example, if each of B,C,D,E, and F of formula I were any of the 20 naturally occurring amino acids there would be over 3 million possible peptides. Hence there is substantial variability in the genus. Further, it is noted that the

claims are open to bioisosteres (claim 3) further increasing the size of the genus. Figure 1 shows 7 compounds. However, as discussed above (see 112 2nd) it is unclear if such compounds are in the instant genus. Even if one considered such compounds as members of the instant genus, such compounds do not represent the substantial variability in the genus.

Since there are a substantial variety of polypeptides possible within the genus, the examples do not constitute a representative number of species and do not sufficiently describe the genus claimed (see Gostelli above).

(3) Physical and/or chemical properties and (4) Functional characteristics:

The agent used for treatment is described as an inhibitor (claim 1) and is also described by functional properties (claims 3,12-14,18). However, there is not adequate direction provided as to what core sequence is necessary for the inhibitory function. There are no common attributes or characteristics that identify the inhibitors or inhibitors that have antagonist activity against C5aR. There is no teaching in the specification regarding what part of the structure can be varied while retaining the requisite activity. Any assays that are described in the experimental section appear to be drawn to a limited subset of compounds (see example 3 page 30). From such data one would not recognize a disclosed correlation between function and structure. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus and that there is a lack of the knowledge in the art regarding which amino acids can vary to maintain the function and thus that the applicant was not in possession of the claimed genus.

(5) Method of making the claimed invention:

The specification (specifically page 21) describes synthesis of PMX53, however the specification fail to describe the synthesis of a representative number of inhibitors and peptidomimetics.

As stated *supra*, the MPEP states that written description for a genus can be achieved by a representative number of species within a broad generic. It is unquestionable that the claims are broad and generic, with respect to all possible inhibitors and peptidomimetics encompassed by the claims. The possible structural variations are many. Although the claims may recite some functional characteristics, the claims lack written description because there is no disclosure of a correlation between function and structure of the inhibitors beyond those inhibitors specifically disclosed in the examples in the specification. Moreover, the specification lacks sufficient variety of species to reflect this variance in the genus. While having written description of inhibitors identified in the specification tables and/or examples, the specification does not provide sufficient descriptive support for the myriad of inhibitors embraced by the claims.

The description requirement of the patent statue requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See *In re Wilder*, 736, F.2d 1516, 1521, 222 USPQ 369, 372-73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate.") Accordingly, it is deemed that the specification fails to provide adequate written description for the genus of the claims and does not reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the entire scope of the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5,8-18,23-24,27 are rejected under 35 U.S.C. 102(b) as being anticipated by Taylor et al (WO 03/033528 as cited in the IDS).

Taylor teach cyclic compounds as antagonists of C5a receptors that are useful in the treatment of inflammatory conditions (abstract) specifically those involving the activation of the complement system (page 55 lines 1-4). Taylor teach that a specific condition to be treated is Alzheimers disease (page 8 line 23-31, claim 23) thus meeting the patient population recited in claims 1-2,23-24 of the instant invention.

Taylor teach numerous compounds for use in the invention and state that particular compounds such as compound 1 have appreciable antagonist potency in a particular assay (page 32 line 11-14). Compound 1 is shown in Table 1 and Taylor teach that compound 1 is also referred to as PMX53 (page 18 line 7-8) and state that PMX53 is represented by Ac-Phe-[Orn-Pro-dCha-Trp-Arg] (page 17 lines 28-29). Taylor also teach the compound PMX205 (page 17 lines 33-35) which is identified as compound 17 on page 40 Table 3 (see also page 34 #17 and Table 3). Taylor teach administration of such compound (see claims 17,20,23) to those with Alzheimers disease. PMX205 meets the structural limitations set forth in claims 3-4,9-18 of the instant invention. Further, since the claims are drawn to peptidomimetics of formula I, PMX205

is interpreted as a peptidomimetic of the compounds recited in claims 5,8 thus meeting the claim limitations. It is noted that the claims state that the compound is a peptidomimetic of Formula I and as such does not necessarily have to be of formula I. Further, other recited compounds such as compound 12 (page 34, claim 17) directly meet the recited structural limitations of claim 5. Further, other recited compounds such as compound 2 (page 22, claim 17) directly meet the recited structural limitations of claim 8. It is noted that particular claims (claims 3,12-14,18) recite properties of the compounds. Since the compounds of Taylor, for example PMX205, meet the structural limitations the functional limitations are necessarily met, absence evidence to the contrary (see MPEP section 2112.01).

Taylor teach the use of more than one of the compounds in the compositions for administration (page 13 lines 1-8) thus meeting the limitations recited in claim 27 of the instant invention.

It is noted that the instant claims are drawn to methods of treatment. The instant specification (page 17 lines 16-30) teach that the term 'treatment' means those that may be prophylactic and that 'treating' includes preventing. Since a method of prevention is used on a patient population prior to the onset of the ailment/disorder, any patient population is available for preventative administrations.

As discussed above (see 112 2nd), the claims are unclear. For purposes of examination, the claims have been given the broadest reasonable interpretation. In particular, the term peptidomimetic has been given the broadest reasonable interpretation such that any compound that shares any similar sequence, for example a single amino acid residue or functional group, is considered a peptidomimetic. Regarding claim 3, the broadest reasonable interpretation is that

X1 is not limited to any particular structure. Regarding the compounds of claims 15-17 the broadest reasonable interpretation is that the compounds of Taylor et al (WO 03/033528 as cited in the IDS) are within the scope of the claims. Regarding the elected species, the broadest reasonable interpretation is that either the structure shown in Figure 1 of the instant invention, or the structure of PMX53 as shown in Taylor et al (WO 03/033528 as cited in the IDS) meet the limitations.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5,8-18,23-24,27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taylor et al (WO 03/033528 as cited in the IDS) and Farkas et al (Journal of Physiology 1998, 507.3 pages 679-687) and Gerard et al (Annu. Rev. Immun. 1994 12:775-808 as cited in IDS).

As discussed above, Taylor teach cyclic compounds as antagonists of C5a receptors that are useful in the treatment of inflammatory conditions (abstract) specifically those involving the activation of the complement system (page 55 lines 1-4). Taylor teach that a specific condition to be treated is Alzheimers disease (page 8 line 23-31, claim 23) as recited in claims 1-2,23-24 of the instant invention. Taylor teach numerous compounds for use in the invention and state that particular compounds such as compound 1 have appreciable antagonist potency in a particular assay (page 32 line 11-14). Compound 1 is shown in Table 1 and Taylor teach that compound 1 is also referred to as PMX53 (page 18 line 7-8) and state that PMX53 is represented by Ac-Phe-[Orn-Pro-dCha-Trp-Arg] (page 17 lines 28-29). Taylor also teach the compound PMX205 (page 17 lines 33-35) which is identified as compound 17 on page 40 Table 3 (see also page 34 #17 and Table 3). Taylor teach administration of such compound (see claims 17,20,23) to those with Alzheimers disease. PMX205 meets the structural limitations set forth in claims 3-4,9-18 of the instant invention. Further, since the claims are drawn to peptidomimetics of formula I, PMX205 is interpreted as a peptidomimetic of the compounds recited in claims 5,8 thus meeting the claim limitations. It is noted that the claims state that the compound is a peptidomimetic of Formula I and as such does not necessarily have to be of formula I. Further, other recited compounds such as compound 12 (page 34, claim 17) directly meet the recited structural limitations of claim 5. Further, other recited compounds such as compound 2 (page 22, claim 17) directly meet the recited structural limitations of claim 8. It is noted that particular claims (claims 3,12-14,18)

recite properties of the compounds. Since the compounds of Taylor, for example PMX205, meet the structural limitations the functional limitations are necessarily met, absence evidence to the contrary (see MPEP section 2112.01). Taylor teach the use of more than one of the compounds in the compositions for administration (page 13 lines 1-8) thus meeting the limitations recited in claim 27 of the instant invention.

Taylor does not expressly teach the elected disease (Parkinsons disease).

As discussed above, Taylor recognize the use of treating disorders that are driven by complement activation (page 2 last paragraph, page 33 lines 1-4) and specifically recite Alzheimers as a disorder to be treated with specific C5aR antagonists (claim 23).

Farkas teach that an abnormal activation of the C5a signal transduction pathway can result in apoptosis and subsequently neurodegeneration (page 679, number 6). Farkas teach that C5a is part of the complement system (page 679 first paragraph). Farkas teach that the involvement of apoptotic cell death in several neurodegenerative diseases including Alzheimers disease and Parkinsons disease has been suggested (connecting paragraph of page 686-686).

Gerard teach biological systems in which complement activation has been suspected to contribute to certain pathophysiologies (page 777 first paragraph and Table 1). In particular, Alzheimers disease and Parkinsons disease (Table 1) are both listed as neurologic systems with evidence for complement activation.

As such, both Farkas and Gerard link Parkinsons disease to activation of the complement pathway. Since Taylor teach treating disorders that are driven by complement activation (page 2 last paragraph, page 55 lines 1-4) one would be motivated to treat specific disorders such as

Parkinsons disease as suggested by the teachings of Farkas and Gerard. It is noted that Taylor specifically teach Alzheimers as a disorder to be treated with specific C5aR antagonists (claim 23). As discussed above, both Gerard and Farkas recognize Alzheimers and Parkinsons as diseases linked to complement activation. Thus, one would be motivated to use antagonists of C5aR as taught by Taylor for those with Parkinsons disease. Since Taylor teach that the compounds are both potent and selective (abstract) one would have a reasonable expectation of success. Taylor states that comments regarding administration are applicable to compound 1 (i.e. PMX53) (page 16 line 30-33) and Taylor specifically uses PMX53 in the examples (see Figures 1,2,3,10,12,13,14 for example). Thus one would recognize that PMX53, the elected species of the instant invention, can be used in the methods of treatment, specifically to those with Parkinsons disease, and one would have an expectation of success based on the data shown in the figures of Taylor and the teachings of Farkas and Gerard. The elected species of PMX53 meet the structural limitations of claims 1-5,8-18 of the instant invention. Parkinsons disease, as suggested by both Farkas and Gerard, meet the specific limitations of claims 1-2,23-24 of the instant invention. Taylor teach the use of more than one of the compounds in the compositions for administration (page 13 lines 1-8) thus meeting the limitations recited in claim 27 of the instant invention.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

It is noted that the instant claims are drawn to methods of treatment. The instant specification (page 17 lines 16-30) teach that the term 'treatment' means those that may be prophylactic and that 'treating' includes preventing. Since a method of prevention is used on a patient population prior to the onset of the ailment/disorder, any patient population is available for preventative administrations.

As discussed above (see 112 2nd), the claims are unclear. For purposes of examination, the claims have been given the broadest reasonable interpretation. In particular, the term peptidomimetic has been given the broadest reasonable interpretation such that any compound that shares any similar sequence, for example a single amino acid residue or functional group, is considered a peptidomimetic. Regarding claim 3, the broadest reasonable interpretation is that X1 is not limited to any particular structure. Regarding the compounds of claims 15-17 the broadest reasonable interpretation is that the compounds of Taylor et al (WO 03/033528 as cited in the IDS) are within the scope of the claims. Regarding the elected species, the broadest reasonable interpretation is that either the structure shown in Figure 1 of the instant invention, or the structure of PMX53 as shown in Taylor et al (WO 03/033528 as cited in the IDS) meet the limitations.

Claims 1-5,8-18,23-24,27-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taylor et al (WO 03/033528 as cited in the IDS) and Farkas et al (Journal of Physiology 1998, 507.3 pages 679-687) and Gerard et al (Annu. Rev. Immun. 1994 12:775-808 as cited in IDS) and Hrycaj et al (Rheumatology v42 May 2003 page 702-703).

As discussed above, Taylor, Farkas, and Gerard render obvious claims 1-5,8-18,23-24,27 of the instant invention.

Taylor, Farkas, and Gerard do not expressly teach the use of the elected second agent infliximab as recited in instant claim 28.

As discussed above, Taylor recognize the usefulness of the C5aR antagonist compounds in the treatment of inflammatory conditions (abstract). Further, taken together the references motivate the specific treatment of Parkinsons disease.

Hryjac teach the adminstration of infliximab to a patient with Parkinson's disease (PD) (1st column, 2nd paragraph). Hryjac teach that infliximab is anti-TNFalpha treatment (1st column, 2nd paragraph). Hryjac teach that the data suggests that TNFalpha blockade may be beneficial in patients with PD (page 702, last sentence of 2nd to last paragraph).

Since Hryjac teach that infliximab is an anti-TNFalpha treatment (1st column, 2nd paragraph) one would recognize that such compound would be useful for the treatment of inflammation such as the patient population of Taylor. Further, since Hryjac teach that the data suggests that TNFalpha blockade may be beneficial in patients with PD (page 702, last sentence of 2nd to last paragraph) one would be motivated to use infliximab for those with PD. Since Taylor, Farkas, and Gerard render obvious administering compounds such as PMX53 to those with Parkinsons disease and Hryjac motivate infliximab for those with Parkinsons disease the

idea of combining PMX53 and infliximab for treating those with Parkinsons disease flows logically from their having individually been taught in the prior art. Such combination would meet the limitations of claim 28 of the instant invention.

As such, all the claimed elements (PMX53, infliximab, patients with Parkinsons disease) were known in the prior art and one skilled in the art could have combined the elements (i.e. PMX53 and infliximab) as claimed by known methods with no change in their respective functions, and the combination would have yielded predictable results to one of ordinary skill in the art at the time of the invention.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references.

It is noted that the instant claims are drawn to methods of treatment. The instant specification (page 17 lines 16-30) teach that the term 'treatment' means those that may be prophylactic and that 'treating' includes preventing. Since a method of prevention is used on a patient population prior to the onset of the ailment/disorder, any patient population is available for preventative administrations.

As discussed above (see 112 2nd), the claims are unclear. For purposes of examination, the claims have been given the broadest reasonable interpretation. In particular, the term peptidomimetic has been given the broadest reasonable interpretation such that any compound that shares any similar sequence, for example a single amino acid residue or functional group, is considered a peptidomimetic. Regarding claim 3, the broadest reasonable interpretation is that

X1 is not limited to any particular structure. Regarding the compounds of claims 15-17 the broadest reasonable interpretation is that the compounds of Taylor et al (WO 03/033528 as cited in the IDS) are within the scope of the claims. Regarding the elected species, the broadest reasonable interpretation is that either the structure shown in Figure 1 of the instant invention, or the structure of PMX53 as shown in Taylor et al (WO 03/033528 as cited in the IDS) meet the limitations.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-5,8-18,23-24 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6,8-10,12-21 (see

8/14/08 claim set) of copending Application No. 10/491,117 ('117). Although the conflicting claims are not identical, they are not patentably distinct from each other.

'117 teach administration of compounds to those with Alzheimers disease (claim 16) thus meeting the patient population of claims 1,23-24 of the instant invention. '117 teach the compound HC-[OPdChaWR] (claim 19) thus meeting the structural limitations of claims 1-4,9-18 of the instant invention. '117 also teach specific A groups (claim 3) thus meeting the limitations recited in claim 5 of the instant invention. '117 teach specific B groups as exemplified in claim 10 thus meeting the limitations recited in claim 8 of the instant invention. It is noted that particular claims (claims 3,12-14,18) recite properties of the compounds. Since the compounds of '117 meet the structural limitations the functional limitations are necessarily met, absence evidence to the contrary (see MPEP section 2112.01).

As discussed above (see 112 2nd), the claims are unclear. For purposes of examination, the claims have been given the broadest reasonable interpretation. In particular, the term peptidomimetic has been given the broadest reasonable interpretation such that any compound that shares any similar sequence, for example a single amino acid residue or functional group, is considered a peptidomimetic. Regarding claim 3, the broadest reasonable interpretation is that X1 is not limited to any particular structure. Regarding the compounds of claims 15-17 the broadest reasonable interpretation is that the compounds of '117 are within the scope of the claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Prior Art of Record

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure: Fairlie et al (WO 99/00406 as cited in the IDS) teach administration of specific compounds (claim 17) for those with Alzheimers disease (claim 21).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to RONALD T. NIEBAUER whose telephone number is (571)270-3059. The examiner can normally be reached on Monday-Thursday, 7:30am-5:00pm, alt. Friday, EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on 571-272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Anish Gupta/

Primary Examiner, Art Unit 1654

/Ronald T Niebauer/
Examiner, Art Unit 1654